Exhibit J

Risk Management: A Regulatory Perspective

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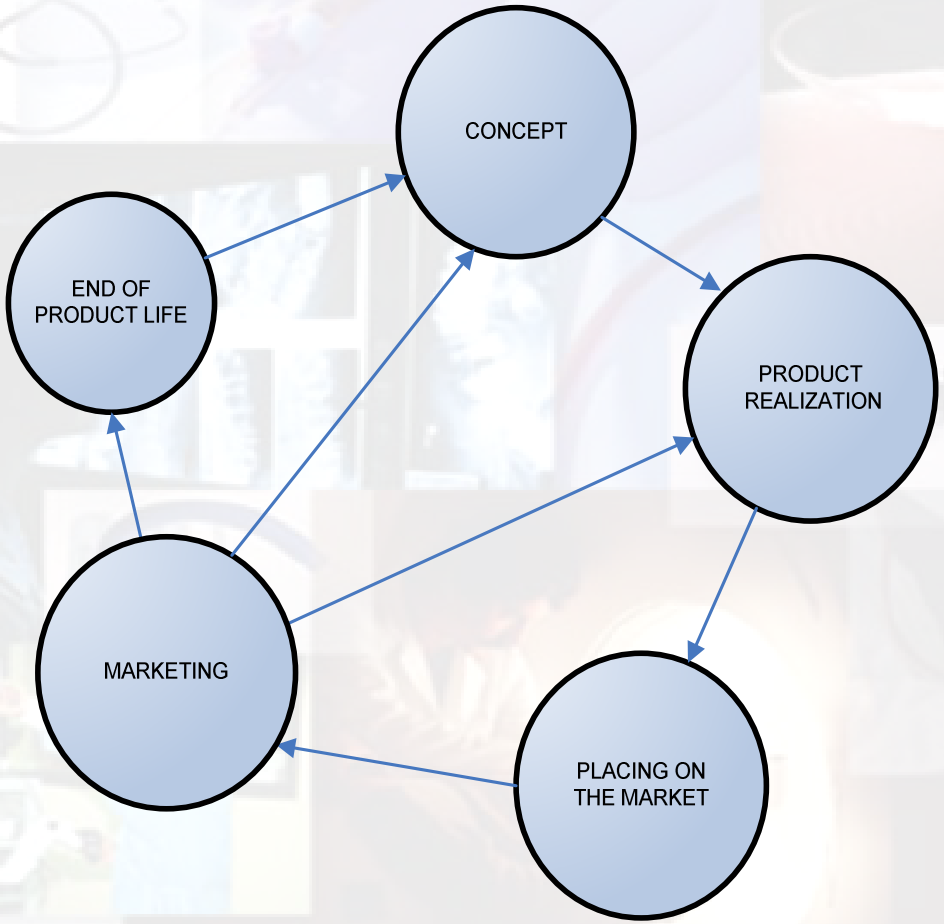
Agenda

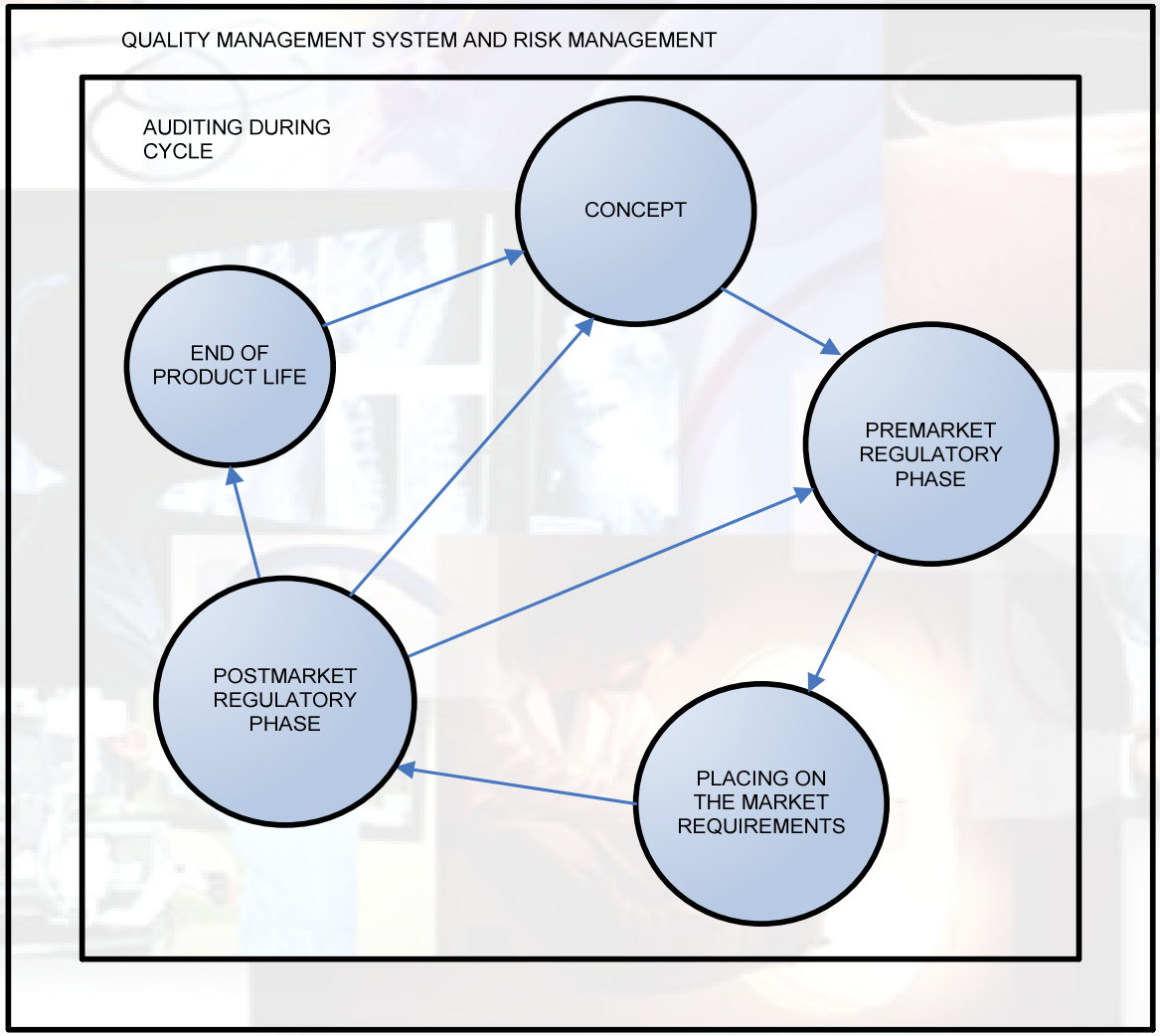
- **Part I: Risk management: A common theme for manufacturer and regulator but different roles during product life cycle**
- **Part II: Risk management external: USA FDA requirements or recommendations for manufacturers and others**
- **Part III: Risk management internal: Regulatory information inputs, assessments, and decisions**

Part I: Common Themes

Life cycle product stages



Life cycle regulatory stages



Risk Management Theme

Risk management is " systemic application of management policies, procedures and practices to the tasks of analyzing, evaluating, controlling, and monitoring risk" *throughout the product life cycle*

Risk being "the combination of the probability of occurrence of harm and the severity of that harm"

ISO 14971/2007 except for italics

Risk Management Theme

In regard to risk management who is it that should (must) apply "a framework within which experience, insight, and judgment are applied systematically to manage the risks associated with the use of medical devices"

The answer: All parties associated with the device during its life cycle. Manufacturers, regulators, users, health care facilities, etc.

Risk Management Theme

We all apply the same concepts in managing risk within the scope of our duties and responsibilities:

- **Risk analysis**
- **Risk evaluation**
- **Risk control**
- **Evaluation of residual risk**
- **Risk management report**
- **Production and post-production information**

Risk Management Roles

- **Manufacturer: Is the device suitable to be placed on the market and to remain on the market considering aspects such as regulatory requirements and risk management**

- **Regulator: Is the manufacturer conforming to premarket and postmarket requirements to ensure proper decisions and actions; Continuous monitoring and assessment**

Risk Management Roles

Manufacturer is primarily responsible for the assurance of safety and performance of the medical device

Depending on regulatory systems and risk of the device, the regulator exerts controls from their legal tool box to confirm premarket suitability and to protect the public health when the manufacturer fails to act, when necessary, in the postmarket phase

Quick voluntary action and collaboration always more efficient than mandatory regulatory action

Part II: External

Risk Management Externally Subagenda

- **Risk Management Provisions**
  - ISO 13485
  - ISO 14971
  - USA FDA Quality System Regulation (21 CFR 820)
- **Risk Based Decisions**
  - Quality System Regulation
  - "Preamble" discussion to the Quality System regulation

Risk Management Externally Subagenda

- **Similarities between ISO and FDA Risk Management Requirements**
- **Evaluation of Risk Management Systems in a Quality System/GMP Inspection**

Risk Management Provisions: ISO 13485

- **7.1 Planning of Product Realization**

  The organization shall establish documented requirements for risk management throughout product realization. Records arising from risk management shall be maintained.

  Note 3 See ISO 14971 for guidance related to risk management.

Risk Management Provisions: ISO 14971

1 Scope

This International Standard specifies a process for a manufacturer to identify the hazards associated with medical devices, including in vitro diagnostic (IVD) medical devices, to estimate and evaluate the associated risks, to control these risks, and to monitor the effectiveness of the controls.

The requirements of this International Standard are applicable to all stages of the life-cycle of a medical device. …

This International Standard does not require that the manufacturer have a quality management system in place. However, risk management can be an integral part of a quality management system.

Risk Management Process: ISO 14971

Risk Management

Risk Analysis
-Intended use/purpose ID
-Hazard ID
-Risk estimation

Risk Evaluation
-Risk acceptability decisions

Risk Assessment

Risk Control
-Option analysis
-Implementation
-Residual risk analysis
-Overall risk acceptance

Post-Production Information
-Post-production experience
-Review of risk mgmt.experience

Risk Management Requirements: USA Quality System Regulation

- **21 CFR 820.30(g) Design Validation**

… The results of design validation shall include software validation and risk analysis …

- **Also Risk Based Decisions to Implement Quality System Requirements**
  - Preamble comments

Risk Management Requirements: USA QS Regulation

Risk Analysis includes:

- **Identification of possible hazards**
  - including use error
- **Risk Calculate**
  - normal and fault conditions
- **Risk Acceptability Determination**
- **Risk Reduced to Acceptable Level**
- **Evaluation of changes for introduction of new hazards**

Preamble Comment 83

Risk Management Requirements: USA QS Regulation

- **Risk Based Decisions in the QS Regulation Preamble**
  - 820.1 Scope
  - 820.30 Design Controls
  - 820.50 Purchasing Controls
  - 820.65 Traceability
  - 820.70 Production and Process Control
  - 820.90 Non Conforming Product
  - 820.100 CAPA
  - 820.200 Servicing

Risk Management Requirements: USA QS Regulation

820.30(i) Design Changes

... Manufacturers must also conduct such tests when they make changes in the device ... The extent of testing conducted should be governed by the risk(s) the device will present if it fails ...

Preamble Comment 81

Risk Management Requirements: USA QS Regulation

- **820.50 Purchasing Controls**

…. the need for specifications should be based on the criticality of and risk associated with the use of the specific manufacturing material.

Preamble Comment 115

Risk Management Requirements: USA QS Regulation

- **820.50 Purchasing Controls (Continued)**

  …. The extent of the specification detail necessary to ensure that the product or service purchased meets requirements will be related to the nature of the product or service purchased, taking into account the effect the product or service may have on the safety or effectiveness of the finished device …

Risk Management Requirements: USA QS Regulation

- **820.90 Non Conforming Product**

  The requirement in this section … requires that nonconforming product discovered before or after distribution be investigated to the degree commensurate with the significance and risk of the nonconformity.

  Preamble Comment 161

Risk Management Requirements: USA QS Regulation

- **820.100 Corrective and Preventative Action (CAPA)**

… FDA agrees that the degree of corrective and preventive action taken to eliminate or minimize actual or potential nonconformities must be appropriate to the magnitude of the problem and commensurate with the risks encountered …

Preamble Comment 159

820.100 CAPA Continued

- **820.100 CAPA (Continued)**

  … FDA does expect the manufacturer to develop procedures for assessing the risk, the actions that need to be taken for different levels of risk, and how to correct or prevent the problem from recurring, depending on that risk assessment …

Risk Management Requirements: USA FDA vs. ISO

- **FDA & ISO Quality Management System Requirements**
  - Require risk management activities
  - Point towards ISO 14971's process
  - Do not mandate ISO 14971

Risk Management Requirements: USA FDA vs. ISO

- **FDA Risk Analysis vs ISO 14971 Risk Management**
  - Intentional Similarities in objectives and process
  - Terminology Differences
    - FDA Preamble: risk in terms of patient & user
    - ISO 14971: risk applies to people, property & environment
  - FDA Risk Analysis ≈ ISO Risk Analysis + ISO Risk Evaluation + ISO Risk Control
  - **Feedback Loops**
    - **FDA – CAPA (see prior slide on CAPA)**
    - **ISO 14971 – Clause 9 Production & Post Production**
    - **ISO 13485 – Clause 8 Improvement**

USA FDA vs. ISO

- **ISO 14971 Clause 9 – a system to collect and review information about device or similar device in production or post production phases; feed back; any changes in risks managed**

- **ISO 13485 Clause 8 - Corrective and preventive action**

Evaluation of Risk Management During a USA FDA Audit

Design Controls

- Ensure procedures document a repeatable, well defined risk analysis process
- Ensure risk analysis procedure has been implemented
- Review Design Output Requirements
- Review Design Validation
- Determine links to other subsystems

Evaluation of Risk Management During a USA FDA Audit

Production & Process Controls

- Review methods for controlling & monitoring the process

Purchasing Controls

- Ensure the role of risk to the patient/user is documented in procedures for evaluation and control of suppliers, and procedures are implemented
- Ensure there are links to other subsystems

Evaluation of Risk Management During a USA FDA Audit

Corrective and Preventive Action

- Ensure procedure(s) document(s) how risk to the patient/user is used to:
  - Prioritize CAPA items
  - Determine the degree to which a CAPA item is investigated
  - Determine depth of root cause investigation
  - Determine the verification and validation activities
- Ensure procedures are fully implemented
- Ensure there are links to other subsystems

Part III: Internal

Internal

In Part II I illustrated the USA FDA requirements for manufacturers related to risk management. The manufacturers receive information, assess it, and take actions as appropriate according to requirements and risk management principles.

How does the regulator assimilate information and take action as needed?

Internal: Postmarket Inputs

- **Mandatory Reporting by manufacturers and user facilities ("MDRs")**
  - Deaths
  - Serious Injuries
- **Corrections and Removals (recalls)**
- **Complaints to regulator**
- **Regulatory Audits by USA or others**
- **Literature**
- **NCAR (GHTF)**

Internal: Postmarket Inputs

- The press
- Bi, Tri- lateral discussions
- GHTF forums
- Website chat rooms
- Medical societies
- Insurance and other government sources
- Medsun
- Submissions
- Import test data
- AND OTHER SOURCES

Internal: Knowledge Management

- **Procedures based on method of reporting to USA FDA, examples**
  - Mandatory reporting of deaths and serious injuries
  - Corrections and removals
- **Creating systems for improving data management, assessment and decisions, examples**
  - Matrix organization
  - Import action plan
  - Internal Quality System

MDR Data Flow and Reporting

Deaths (all), Serious Injury (when mfr unknown) - **10 work days**

User Facility

Death & Serious Injury - **10 work days**

Importer — D & SI →

Death, Serious Injury & Malfunctions - **30 calendar days**

FDA

Other Sources

Deaths & Serious Injuries

Product Problems/ Malfunctions

Remedial Action w/ unreasonable risk harm or FDA requested - **5 work days**

Death, Serious Injury & Malfunction **30 calendar days***

Manufacturer

Internal: Corrections and Removals

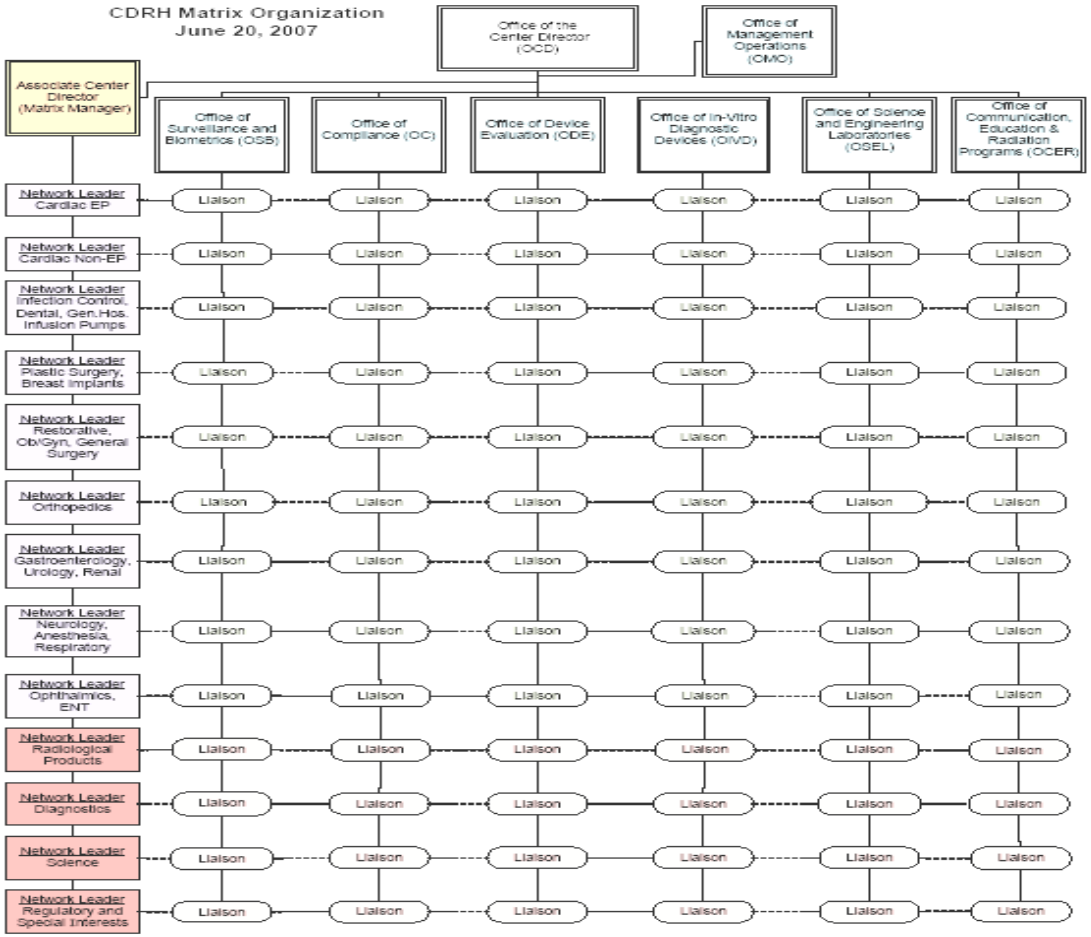
Manufacturer:

- **Corrects a device on the market**
- **Removes a device from the market**
- **Submits a report to USA FDA if the product presents a risk to health or does not meet legal requirements (not cleared, defective, mislabelled)**
- **A "RECALL"**

Internal: Recall Process

- Manufacturer takes action and makes report
- USA FDA classifies the recall based on risk assessment process: Class 1, 2, 3
- Internal feedback on recalls to premarket program

Internal: Matrix Organization



Internal: Import Action

- **Improved Data Systems and decision support using multiple sources of data**
- **Leveraging audit information globally**
- **Collaborations between competent authorities**
- **Risk-based foreign audit programs**

Internal: Quality System

- **Internal organization and processes based on ISO/QS regulation principles**
  - Quality Management System
  - Management Responsibility
  - Resource Management
  - Work Processes, Controls, and Execution
  - Quality Measurement, Acceptance and Improvement

SUMMARY

- Common themes, common fundamental approaches
- External requirements relating to risk management
- Internal processes to manage risk